THE MÜTTER LECTURES ON SELECTED TOPICS IN SURGICAL PATHOLOGY.

SERIES OF 1890-1.[1]

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LECTURE IV.

THE RESULTS OF THE ABSORPTION OF THE PRODUCTS OF WOUND INFECTION.

Syllabus.—Surgical Fever. Intestinal or Enteric Toxæmia, and its relation to surgical cases. Sapræmia or poisoning from "Septic Suppositories." Septicæmia. Pyæmia; idiopathic or spontaneous; from causes unexposed to the external atmosphere; from old inflammatory foci. Spontaneous suppuration in previously healthy persons. Resumé of Rinne's experimental researches concerning production of sepsis.

FOR PRESENT purposes and in the light of the pathological knowledge of the day, I propose to group under five distinct headings the various septic disturbances which may result from injury or wound, which in time past have been variously regarded and classified, and which furthermore have been all summed up by the laity under the comprehensive, yet inaccurate name, blood-poisoning. These five forms are as follows:

  1st. Surgical fever.
  2nd. Intestinal toxæmia.
  3rd. Sapræmia.
  4th. Septicæmia.
  5th. Pyæmia.

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First. Surgical fever.—Under the term surgical fever, asep-
tic wound fever or fermentation fever, are included those im-
mediate febrile disturbances which result in two or, at most,
three days after an injury or a wound. This form is charac-
terized mainly by pyrexia, with only so little nervous, emo-
tional or digestive disturbance as seems always to accompany
the same grade of pyrexia. It was called fermentation fever
by Bergmann because it was supposed to be due to the fer-
mentation of some fibrinous substance, or to be connected in
some way with the fibrinous ferment. It has been shown by
numerous observers that the introduction of blood into healthy
animals by transfusion would produce a rise of temperature,
indeed intravenous injections of clear water, or of salt solution,
have the same effect, as do also injections of aseptic emulsified
substances, such as water containing finely pulverized char-
coal, in suspension. Bergmann further showed that such a
fever may also be produced by intravenous injections of pan-
creatin, pepsin and trypsin. It would appear further that
albuminoid substances when undergoing oxydation occasion
rise of temperature, which proceeds until the products of oxy-
dation are eliminated through the kidneys. The most proba-
ble and most satisfactory explanation of surgical fever is that
it is due to the trifling disturbance attending absorption of
minute products of aseptic tissue necrosis, or the oxydation or
metabolism of the same. It is not always met with, and may
vary in degree according to the age and condition of the subject.
It speedily subsides by lysis, and has in it absolutely noth-
ing implying sepsis, nor is it anything except a phlogenic con-
servative process.

Second. Intestinal toxæmia.—I give this topic a distinct
caption of its own because I am very sure its importance is al-
ways under-rated by students and junior practitioners, and of-
ten by their seniors, as by writers generally. Indeed, under
this term are included conditions which, perhaps, deserve to
be grouped separately, though as yet we lack such accurate
knowledge as shall permit a proper classification. Intestinal
sepsis or *enterosepsis* has, indeed, been mentioned by Billroth,
and by other writers, and yet it has been difficult to determine
precisely what they meant by these terms. *Enteritis septica*

is described by Gussenbauer, but it is hardly the term to apply to the condition now under consideration. Under this caption, then, I include, 1st, a condition of unusual, or at least undesirable activity in the contents of the intestinal canal, by which, whether due to common or specific forms of bacteria, the ptomaines of putrefaction are produced in such manner, or such quantity, that they are absorbed through the intestinal mucosa, and distributed over the body, by which a condition of intoxication is produced. In this form it is not meant to imply that any of these bacteria gain access to the circulation, only that a more or less profound toxæmia is produced. 2nd, a form in which the common or uncommon bacteria met with in the intestinal canal pass into and infect the living tissues of the patient, and produce local or general infection in addition to the toxæmia above described. That the first form occurs alike in surgical and medical cases I think no one will deny. That the second form is possible, if not common, is made sure by such researches as those of Karlinski. He fed animals with milk infected with staphylococcus aureus. Among forty-eight experiments he found six times general infection with swelling and reddening of the intestinal mucosa, while the fæces and the blood both showed the same cocci. Five times he found suppurative parotitis without intestinal lesions; seventeen times acute and fatal diarrhœa; eight times general infection with metastatic abscess. (He often noticed an increase of virulence after passing these cocci through these animals.) (*Prager Med. Woch..* 1860, No. 22.)

Aside from these experiments of Karlinski, there are numerous other observations all tending to show that the most common inhabitant of the alimentary canal, the *bacterium coli commune,* may be taken up by the intestinal absorbents and conveyed to at least neighboring points, where it may set up abscess with its attendant symptoms. It is extremely probable also that other intestinal organisms may take the same course. In this way, for instance, are to be explained the abscesses in the liver which accompany or follow dysentery, and in which living organis.ns have been described by Kartulis, by Osler and by others.

A very careful study of the pathological and infectious properties of the bacterium coli commune has been very recently published by Tavel, of Berne. (*Corres. Blatt. f. Schweizer Aerzte.* Juli, 1889, page 347). It was in 1878 that Kocher emitted the idea that suppuration of goitrous tumors was due to a secondary infection from the intestine, consecutive upon an enteritis. Tavel, studying two such cases carefully, was able to obtain pure cultures from the pus of a bacillus which produced gas, and which closely resembled bacteria of the large intestine. These he described in 1887. During the present year he had opportunity to study yet another similar case. In February there was operated upon an enormous goitrous tumor composed of two cysts; one of these was completely enucleated, the other partially so. During the operation there was a violent hæmorrhage which was checked by pressure with sponges. Some hours later there was collapse, and infusion of salt solution for the relief of the traumatic anæmia was practiced with success. A little later, on account of secondary hæmorrhage, the dressing was removed and compression with sponges again practised. The next day the drain was removed, as usual in Kocher's clinic, and was placed in jelly without developing any colony until after it had been present several weeks, when there developed a small coccus which did not liquify the gelatine. In the meantime cicatrization of the wound as complete, when there presented a hæmatoma which called for puncture. At this time two cultures were made from the blood of this cyst; one of these developed a pure culture of a short bacillus, which by accurate comparison was positively identified as the bacterium coli commune. The subsequent course of events in this case was very different from that of a mixed surgical infection. The walls of the hæmatomatous cavity became necrotic, but secreted neither serous fluid nor pus. When this cavity was scraped out later, there was removed a small fragment of sponge. Strange to say the sponge contained no bacteria, nor did the fragment removed, and the question is, did the bacteria of the large intestine reach the spot through the circulation, or did they spread there through the skin. Tavel seems to be of the opinion that in this case they reached the wound at the time when the infusion was practiced. Nevertheless, that the bacterium coli commune may become pathogenic, and, proliferating in the blood, spread to the intestine, the same author has made certain by a series of experimen s, since after intra-venous injections numerous animals died, and in all their organs were found large numbers of these organisms. Even subcutaneous inoculation was enough to cause death in numerous instances. Such cases as Tavel's at least demonstrate the possibility of a rare complication of wounds, and illustrate especially the necessity of paying particular attention to the intes inal canal both before and after operations.

This second form, however, is much less common than the first, and need not long detain us at present. It is especially to the disastrous results of the detention in the alimentary canal of excrementary material to which I desire to call attention now. It unquestionably brings about a condition of pyrexia, of disturbed secretion and excretion and brain action, and of wound healing, which may at times be mistaken for sapræmia or septicæmia, which may by reasonably intelligible processes be converted into one or the other of these forms,

and yet which it is necessary to sharply distinguish from them. For instance, a patient with a trifling or a serious wound passes the period when we may reasonably expect a conventional amount of surgical fever, and then, owing to inattention or ignorance, permits the bowels for some days to accumulate material which should not have been retained. As a consequence of the putrefaction of this material ptomaines or leucomaines, or other toxic substances, are formed, whose absorption is favored by their retention. That the patient is thereby poisoned is soon evidenced by mental hebetude or ex·citement, by pyrexia increasing in degree, by fetor of the breath, by furring of the tongue, as well as by other well-known and easily recognizable signs and symptoms. Fear of blood poisoning being aroused, the region of the wound is now examined. Unless this condition has advanced too far there will be found here little or nothing to explain the evident signs of poisoning. Should now inquiry be directed toward the condition of the bowels, most significant information will probably be gained, acting upon which a laxative enema cathartic, or both, will be administered, and with the expulsion of the poisonous material the unpleasant symptoms will speedily subside. How often has this been the experience of every practitioner and, yet, how insufficiently has he reflected upon it!

It would be a mistake, however, to suppose that only when a history of constipation is obtained can this condition of affairs result. It often happens, from causes not understood, that there takes place within the intestinal laboratory such a putrefaction as produces ptomaines which are at the same time toxic and cathartic in their action, so that the irritating material is expelled by virtue of the very poisons which it has produced ; and it furthermore often happens that the exhibition of a vigorous cathartic, for instance, one of the mercurials, will so admirably clean out the entire intestinal canal, that not merely is this entire toxic action prevented or checked when present, but that a most happy effect is exerted upon septic disturbances commencing elsewhere.

I regard this intestinal toxæmia as a subject of immense importance, further, because I am convinced that a condition

which begins as a disturbance of this kind may become merged into one of the more serious or septic conditions to be mentioned soon, thereby flooding the area of the wound with organisms introduced directly from the alimentary canal, or so depressing the vitality of the patient as to permit true putrefactive or pyogenic infection from without, when this would not otherwise have occurred. In this connection it is of value to recall that particular function of the liver which has been termed its depurative action, by virtue of which it filters out from the portal circulation those elements which are harmful or toxic to the general economy. It will thus be seen that its role in preventing intestinal toxæmia is a most important one and that if it be prevented or impeded in its action the patient must suffer in proportion. The advantage then to the surgical patient of a healthy liver is simply inestimable, and the beneficial action of a vigorous cathartic administered before an operation, and, perhaps, occasionally after it, by which the function of the liver is stimulated and its canals unloaded, may be the better appreciated.

So far as differential diagnosis between this condition and those to be spoken of, is concerned, it must be based on, first, the general, and second, the local condition of the patient. If there be evidences of poisoning which can be traced to the wound, the trouble may well arise there ; while on the other hand, if the wound be healthy without any evidences of lymphangitis or cellulitis, and without odor or retention of secretion, the explanation is presumably to be sought for elsewhere. Finally, in case of *doubt* the administration of a cathartic will probable settle the question. (*Vide* also the topic of stercoral intoxication at close of Lecture III.)

Third. Sapræmia.—This term was introduced by Mathews Duncan and seems to fit the case as well as any one of the numerous expressions intended to imply the condition. Such other terms as putrid fever, putrid intoxication, etc., are as expressive but not as elegant. Perhaps the best definition of the term can be conveyed by an illustration of the condition itself, and for this purpose none will serve better than that physiological operation of nature's own performance, namely, the act of parturition. By the completion of this operation there

is infl'cted a fresh and bleeding wound of large area, which is more or less exposed to putrefactive agencies. By the comclusion of the act and the contraction of the uterine walls there is left a comparatively small cavity which must contain a small amount of freshly coagulated blood.It is unnecessary to speak of what occurs when the puerperal state is passed without incident, but let us suppose that on the third or fourth day the patient is found with a flushed face, dry tongue, some mental disturbance and a considerable degree of pyrexia, while we are informed that the lochial discharge is altered both in appearance and in odor, the latter being now offensive. The ex· planation of affairs is very simple. Germs of putrefaction which were introduced by carelessness during the act of labor or afterward, have lodged in the contained blood-clot, have caused putrefactive processes, as the result of which ptomaines have been formed. We have then a condition of putrefying and poisonous blood·clot contained within a mass of tissues in which changes and absorptive processes are rapidly taking place; in other words, within a locality where absorption is highly favored. The condition being recognized an antiseptic douche is administered, and frequently repeated, by which means putrefaction is not merely checked, but abolished; and, the source of poison being removed, the natural recupeʳative powers of the patient enable her to recover within a few hours from the dose of poison received.

In this case we have had to deal with putrefaction occurring within a body cavity, and yet not involving the living tissues of that body. In other words just such a poisoning as might occur if we were to take rotting blood-clot and deposit it in a pouch under an animal's skin. Precisely such a condition of affairs occurs in surgical work. In an amputation stump a certain amount of bleeding has occurred, due, perhaps, to insufficient hæmostasis or to lack of proper quietude after the operation. This clot becoming first infected from a failure in antiseptic practices, begins to undergo changes in a precisely similar manner, and the patient to show signs of poisoning. If now these be recognized in time, and antiseptic irrigation with adequate drainage be established, the harm already done

can be quickly undone, while the patient has suffered only a temporary toxic excitement.

In the writer's estimation it would be well to limit the term sapræmia to just so much disturbance as is included in the above illustrations, and to extend it no further. Just so soon as the putrefactive action extends from the contained clot to the containing tissues, the case should cease to be considered one of sapræmia, and should now be regarded as one of septicæmia. It is necessary then to add to the above statements only this, that a distinct form of intestinal toxæmia may become converted into one of sapræmia, simply by a continuation of the orginal condition which predisposes to the other.

Fourth. Septicæmia.—For the writer the difference between sapræmia and septicæmia is not one of character so much as of location. The idea conveyed by the term sapræmia is intended to be that of a putrid suppository, if one may introduce this illustration, from which absorption is continuously taking place; whereas in a case of septicæmia the putrefactive action is no longer confined to material enclosed by, yet strictly speaking without the tissues, but has spread from this to the tissues themselves. Pursuing our previous illustration still further, let us suppose that the recently delivered uterus has contained for some hours its putrid intra-uterine suppository of breaking down material. Presumably by the deleterious action of the poisons therein produced the vulnerability of the tissues has been so far lowered that they no longer resist the action of the micro organisms present. So soon as these have begun to attack the still living tissues, their action is, at least within certain limits, progressive; not so much by means of the circulation as by means of the continuity of tissues, the systemic poison all the while being intensified. So rapid may be this action, as it seems to be in many malignant diphtheritic cases, that the individual speedily succumbs before many evidences of abscess or local gangrene can appear. Or on the other hand providing that the toxic action be less pronounced or the patient's vitality more enduring, or providing also, which amounts to the same thing, that his tissues are more resistant locally, then abscess or local gangrene may result, the destruction of tissue being limited to the part first involved. Should

this have been the uterus this favorable local destruction is less likely to occur, but should it have been in an extremity a natural separation or a mutilating operation may be the means of saving the patients life.

From what has been said, it will be seen how easily a case originally sapræmic may become merged into one of true septicæmia; but it is not intended to imply that the sapræmic condition must always preceed, since many cases begin as pronounced septicæmia from a local infection. When we have to deal with a retained and putrefying blood clot, the case is usually of the former character, but when with a direct local infection, as for example, a dissecting wound, it is usually septicæmic from the beginning.

Fifth. Pyæmia.—The distinction between septicæmia and pyæmia also is one not of toxæmia, but of the formal progression of a series of embolic disturbances, which give rise to the formation of metastatic foci and abscesses, along the lines so well laid down by Virchow. Just what it is which *determines* the formation of minute thrombi and their dislodgement and transportation first to the lungs and later to the system at large, we have not yet determined. Still, so far as can be seen, the distinction between purely local ravages such as those implied in a typical septicæmia and the dissemination over the body of hundreds or thousands of minute, infected emboli, which is comprehended in the term pyæmia, is a matter not clearly understood. It may be pure accident, or it may be something not yet clearly grasped by our apprehension; at all events it scarcely seems to be due to any pathogenic differences in the bacteria involved, for, so far as we at present can see, precisely the same organisms may produce at one time the former character of disturbance, at another the latter. Nor is the matter cleared up by a post-mortem examination of the parts primarily involved, since we are quite likely in each case to find the local veins more or less filled with clotted or semi-clotted blood, with everything favorable for its transportation to all parts of the body. It is scarcely enough to say that we have rather a phlebitis to contend with in the latter case than in the former, since that would imply that in the latter instance

the walls of the veins are more easily permeable by the bacteria at fault.

It is acknowledged that in the above description of these various forms their more typical manifestations have alone been utilized. That intermediate or mixed forms are frequently met with is distinctly acknowledged by the introduction into literature of such expressions as *septico-pyæmia*, *pyo-sephthæmia*, etc. The term *kryptogenetic pyæmia*, introduced by Wagner, scarcely has any place now, inasmuch as we cannot conceive of any form of surgical sepsis which is not kryptogenetic in its etiology.

Few subjects, if any, have more deeply engaged the attention of surgical pathologists than those included under these above headings, and to attempt to summarize the literature and the views of the past, would be to lay before you a work at least no smaller in volume than the scholarly treatise of Gussenbauer. Nevertheless, with the introduction of bacteriological studies into surgical pathology, new phases of old questions have been presented and a vast amount of laborious research has been devoted to illumining them. Since Koch's masterly and path-breaking treatise on the infectious diseases, no original work has appeared upon the subject so creditable in its attacks, and so replete with experimental investigation, as that of Rinne, to which we purpose to give some attention in detail.—*Archiv. f. klin. Chir.*, Bd. 39.

The term Pyæmia was first suggested about fifty years ago by Piorry, and was used by him and others in the old humoral sense. Later the name was continued by Virchow though retained in a revised meaning. With such revised views, with the introduction by Recklinghausen of the term *embolus*, and with a recognition of the possibility of *capillary emboli*, the phenomena of metastasis became susceptible of easy explanation. That bacteria, introduced through respiratory or alimentary passages, or some open wound however small, or carried by the body juices from some local infection, are important contributing agents in this process, is a matter of much more recent development. We have learned furthermore that while it is within their province to thus provoke suppuration, deep or superficial, mild or fatal, there must be certain

favorable disposition of the fluids or tissues to permit such action. We may say that their resistance is lowered; we may call it reduced vitality; we may call it vulnerability;— it matters comparatively little so long as we appreciate the fact.

While we are yet blind to all that constitutes this predisposition we may yet recognize certain conditions as predisposing to suppuration; *e.g.,* subcutaneous injuries, extravasations of blood, presence of foreign bodies, etc. We all acknowledge the existence of *loci minoris resistentiæ,* but can explain very few of them. The endeavor to account for them leads one into a very wide and yet untrodden territory.

As showing what emboli may do, take the following illustrations:

Fraenkel made a very careful study of two cases of sepsis taking its origin from the pharynx. One was a case of pericarditis and double pleurisy. The exudate at first sero-fibrinous, later contained the streptococcus pyogenes. Endeavoring to explain its occurrence in these closed cavities he maintains that organisms, aside from that of tubercle, can reach pleuritic exudate in either of the following ways:

1. When the pleuritis is of an embolic character and when the emboli are already infected.

2. When bacteria are or can be recognized in the blood.

3. When the pleurisy is the result of inflammation spreading from a neighboring infected area by continuity of tissue, and along the lymph vessels which spread to the pleura.

In his first case thus studied there were extensive diphtheritic pharyngitis and laryngitis, followed by a large retro-pharyngeal abscess, which later involved the right tonsil and then spread into the posterior mediastinum. Consequently here the infection was according to the third method mentioned above. At autopsy the same streptococcus alone was found in all the lesions.

In the second case a provisional diagnosis of endocarditis ulcerosa was made. At the autopsy there were found widespread diphtheria of larynx and pharynx, purulent infiltration of the tonsils and their neighboring tissues, myo· and endocarditis diphtheritic, hepatisation of both lungs (catarrhal pneumonia) and large white kidneys. Streptococcus pyogenes was found in the tonsils, the lungs, the diphtheritic membrane, on the inner surface of the heart and in the capillaries of the kidneys.

He compares these ca·es with those reported by others where the pharynx was apparently the port of entry for septic organisms. For instance, Gerhardt's case of facial erysipelas, which proceded from the tonsils, and cases of streptococcus invasion following scarlatina reported by, among others, Löffler, Heubner-Bahrdt, and Freudenberg

Wagenmann has reported a case of puerperal fever, in which total blindness occurred within a few hours. Dissection demonstrated pyæmic foci in various organs. Multiple, extensive emboli of the vessels of each eye were found, the emboli consist-

ing of masses of streptococci. After rapid proliferation inside the vessels these cocci escaped from their walls and were met with free in the retina, vitreous, etc. Furthermore, wherever the cocci were found was found also pus. The former were not found without the latter.

Rinne makes a clinical division of cases of suppuration and general sepsis which has much to justify it, though the minute causes may not vary correspondingly.

1. Metastatic abcesses which occur in a typical way without visible or known external injury or lesion. Spontaneous pyæmia.

2. Pyæmia and septic cases with a recognizable and causative lesion.

3. Subcutaneous suppuration at points where there had previously been inflammation; *e.g.*, abscess following *brisement force* of a joint anchylosed from a former rheumatic attack. A case to belong in this group must be absolutely free from any lesion, however slight, of any part of the surface.

I. *Idiopathic pyæmia.*—Perhaps our best illustration of so-called idiopathic pyæmia can be met with in a case of spontaneous acute infectious osteomyelitis. There is perhaps no disease of whose bacterial origin we are more certain, and we are familiar with all the microbes which have the power of producing it, yet why they select the osseous system, or rather certain parts of it, *i.e.*, usually the diaphyses of long bones, for their attack is a question which we can not yet answer satisfactorily. Or, with Rinne, let us frame this question a little more accurately: Why are the bones selected in such a case as the above, when in a general infection with equable distribution of the blood every tissue enjoys apparently equally good opportunities? Such a question misleads, however, if one takes it for granted that all parts of the body are equally liable to invasion by any given organism. Grawitz especially has shown that there is no bacterium which manifests no preference for one tissue or organ over another. Tubercle, *e.g.*, affects commonly the lungs, liver and bones, relatively seldom the testicles or ovaries, and very rarely the salivary glands or muscles. The same organ may be exempt at certain periods of life. The brain in childhood, especially the meninges, is a

frequent seat of tubercular disease; in adult life rarely so, since it usually escapes in cases of acute general miliary tuberculosis. The bone marrow and synovial membrane are frequently affected in childhood, in adults they commonly escape, though in the acute miliary tuberculosis of adults the bone marrow is again a point of predilection.

Measles and leprosy affect especially the skin, gonorrhœa involves only certain mucous membranes, typhoid fever certain intestinal structures, glanders the skin and lymph-glands, and so on through the list of infectious diseases. In tuberculosis the vascular peculiarities of pia, which is especially rich in lymph vessels, or of the synovialis, may be of effect, or the more torpid circulation in the liver, but such hypotheses as these seem insufficient when we recall that whole systems, like the muscular, including the heart, escape.

It appears then to be a natural law that every disease germ has a preference, so to speak for particular tissues and organs, although of the explanation of this fact we are profoundly ignorant. Only by an overwhelming infection, or when the normal energy of the tissues and cells is altered, is this law set aside. Viewed in this light indiscriminate metastases are violations of this law.

Among all the defensive powers of the system the capability of resorption is perhaps the most important protection enjoyed by the cells and tissues comprising the organism. This power seems to be enjoyed in the highest degree by the peritoneum, which is known sometimes to tolerate and dispose of relatively large amounts of infectious material. Grawitz and Rinne have shown how many pyogenic cocci can be introduced into the peritoneal cavity without inducing peritonitis, provided only—and this is very important—the wound made in performing the experiment is properly disinfected and made to heal *per primam*. The resorptive powers of the unbroken peritoneum are therefore very great. (Vide Lect. V.)

Experiments which lead to a contrary conclusion are to be accounted for by a failure to protect the peritoneal wound. Practicing surgeons are now availing themselves of the lesson thus taught, and are closing peritoneal wounds with great caution. That the peritoneum is by no means suppuration proof

thousands of autopsies have shown; on the other hand, that the healthy, uninjured peritoneum has marvellous powers of absorption of septic germs has been equally proven by hundreds of experiments. Between the two statements there is no discrepancy; it is simply a question of its disturbed or undisturbed condition.

The next most important self protection manifested by the organism is in the degree of concentration of its albuminous fluids. Pyogenic cocci can not thrive in highly albuminous liquids. Upon a mixture of equal parts of gelatine and blood clot they scarcely grow, and in a similar mixture of pus and gelatine they do not develop (Rinne). The explanation of the measure of success attained by means of the "open method" of dressing wounds is hereby furnished; the fluids which exude from the exposed wound surfaces are too rich in albumen for pyogenic or saprogenic action to occur.

As the third variety of auto-protection we must—with some misgiving—mention *phagocytosis*. A discussion of this much vexed matter would lead too far from the present inquiry; consequently, as it has so much about it that is plausible and attractive, I must simply take the ground that it is entitled to enumeration here until its occurrence has been positively disproved.

In the combination of these three defensive capabilities we find the means by which the body, by its component parts, rids itself of the offensive germs, that is when such defense is wholly successful. When successful only to some extent it is because some part, large or small, has been sacrificed to save the balance. The portion thus yielded to the enemy is now dead, and nature at once provides for its extrusion. Under circumstances included in our investigation this extrusion is brought about either by abscess or by sloughing.

Certain well known conditions conspire to prevent defensive action on the part of the tissues, particularly severe complicating general diseases, such, e.g., as typhoid. Such a disease saps the vitality from our cells, and interferes with, if it does not inhibit, their proper function.

A condition of *predisposition* is everywhere recognized and nowhere defined or explained. Still when we keep in view the

varying degrees of virulence which can be demonstrated in certain bacteria artificially cultivated, we can, perhaps, ascribe more or less of the so-called predisposition of our tissues in reality to varying degree of pathogenic potentiality in the bacteria which invade them. For instance it is well known that tubercle as well as anthrax bacilli need to be passed through a living animal body at least as often as every fourth culture in order that they should preserve their virulent powers. Whether in this way their "animosity" against animals is excited, or whether their ptomaine-excreting power is increased, or whether one necessarily implies the other, is more than one can say.

Under ordinary experimental circumstances it would appear to be necessary to inject such a quantity of the common pyogenic cocci that with them should be inserted an appreciable amount of their ptomaines in order to call forth in the animal injected any sign of more than trifling disturbance. Even when the blood of a patient is swarming with these cocci the distinctive features of pyæmia (*i.e.*, metastatic abscesses) are exceptional, and the case is usually one of septicæmia. The nearly if not absolutely complete identity of acute osteomyelitis with pyæmia can be explained by the peculiarly confined limits within which their rapid growth is pent up. Again when richly lymphatic structures, as *e.g.* the lymph glands, are involved in a septic process we see how easily microbes may gain access to the blood, and how quickly the whole body may be affected. Conversely we see also how the lymph glands must act as neighboring filters for lymph vessels which are carrying away from the given lesion the absorbed infecting materials, and why they are very easily involved and often suppurate. No matter if chemical products of bacterial growth, or alkaloids isolated from putrid material, have been known to cause suppuration, they have never been known to cause metastatic abscesses. Many dogs have succumbed to doses of filtered cultures; they have died of toxæmia, showing somnolence, diarrhœa, collapse, etc., but there *never* have been found in their bodies any metastatic abscesses. All this goes to prove that pyæmia is something more than excessive ptomaine poisoning. The fulminating septic symptoms thus pro-

duced by Panum and v. Bergmann had nothing of the anatom-
ical picture of pyæmia about them.

II. *Pyæmic and septic cases with a recognizable and causa-
tive lesion, unexposed to the atmosphere.*—A typical case of this
kind would be a suppurating subcutaneous fracture, such as
Volkmann has described (*Beitrage zur Chirurgie*), or a sup-
purating goitre. In such cases we only need to find the port
of entry of the pyogenic organisms in order to explain the
rest.

Rosenbach, Passet, Krause and Wyssokowitsch, among
others, have shown that when the blood is laden with infec-
tious bacterial material, it needs usually only some subcutane-
ous injury to constitute the *locus minoris resistentiæ.* I say
usually because Rinne found that even after injecting very
large doses of staphylococcus cultures into the peritoneum frac-
tures made subsequent to the injections healed as usual,
although even the injections were contined day after day.
Whether in his experiments the blood of the animal injected
was found to be germ-laden he does not tell us.

Rinne further details a number of experiments in which
numerous and repeated injections of pure cultures into veins
or tissues failed to produce any sign of suppuration, or of dis-
turbance of union in fractured bones; and he claims—undeni-
ably—that mere presence of bacteria is not enough, that we
must seek yet further for the explanation of suppuration and
sepsis in cases belonging to this group. And although it
seems to make a difference what kind of animal is experi-
mented with, and while consequently man may be more
vulnerable than some other animals, yet it is quite in ac-
cordance with our experimental experience that in our clinical
surgery we may find surprises of this character equally signi-
ficant.

A parallel is found in the results of the experimenters (Orth,
Wyssokowitsch, Prudden) who have found that an artificially
injured aortic valve creates a local predisposition for the germs
of malignant ulcerative endocarditis. This injury is in effect a
lesion of the tunica intima, and this seems everywhere to have
the same effect.

But it is undeniable that such subcutaneous injuries as those

above alluded to do create vulnerable points of attack for any micro-organisms circulating in the blood, even though these latter may not always take advantage of them. When bones are broken soft tissues are usually also torn and bruised. How is it that we find the suppuration usually in the bone, rather than in the surrounding muscle? Possibly it may be that the vessels of the soft parts are more crushed than those of the bone, so that the bone wound is more likely to be flooded with bacteria than any other region. Or is the warfare of the cells more actively waged by those of the soft tissues? To my mind it is a combination of both.

Experiments failing to clear up these important problems, we may yet endeavor to discover the exact role played by the chemical products of bacteria, and to see if we can trace any mutual relationships between bacteria, ptomaines and wounds, by which blood poisoning resulting from infection of a point of least resistance can be explained.

The experimental work of Grawitz, de Bary, Scheuerlen and Fehleisen has demonstrated that beside the invasion of the tissues with swarms of bacteria, there is a simultaneous action of their toxic products, which either actually results by itself in production of pus or else permits their rapid growth. It it not so much a question now as to whether injections of cadaverin, as perhaps the best known of the ptomaines, can under unusual circumstances lead to pus formation. Still less is it necessary to show how such active chemical agents as turpentine or ammonia may lead to the same result by themselves, causing a toxic action, or by inhibiting the normal chemical activities of physiological fluids, or by producing gangrene of the skin and favoring bacterial infection from without, or by so preparing the soil that its vital resistance is greatly lowered.

Clinical surgery has ordinarily no such lesions to encounter as those caused by such laboratory experiments. Rinne set himself an experimental task in which he tried to ascertain the activity of such chemical poisons as take part in the inflammatory and septic process and to learn whether they alone can cause suppuration or whether they simply favor the action of bacteria. These experiments were made with:

1. Sterilized fluids in which staph. aureus and albus, and streptococci had been cultivated and then killed by heat.

2. Sterilized putrid fluids, such as that from putrefying meat, etc. These were carefully filtered and cooked, and tested before use.

3. With Brieger's cadaverin.

They were moreover conducted with a view to ascertaining whether these substances produced either inflammation or suppuration in normal, freshly injured or cicatricial tissue or around foreign bodies.

His results briefly were as follows: Injections of sterilized staphylococcus cultures and putrid fluids into healthy subcutaneous tissues, with due precautions, do not produce pus. Even inflammatory reaction was usually absent, and he never made an abscess. Subcutaneous wounds with ecchymoses did not suppurate. He inserted shreds of wool and left them a month, and still such injections made in their proximity failed of pyogenic effect. Even when these threads were soaked in such fluids the result was the same. Equally negative was the result of injections into old cicatricial tissue. Inflammatory signs were in some instances evoked, but resolution quickly followed. After injection of large quantities of sterile staphylococcus cultures abscesses whose pus (?) was free from bacteria were a few times noted, but more often resolution occurred. After introduction of equally large doses of sterile putrid fluids necrosis sometimes occurred, which would naturally be followed by bacterial invasion. Sterile abscesses following these latter were not seen.

Worsted threads soaked in these fluids, and then variously introduced and into various tissues, gave rise for the most part only to inflammatory exudate around them, which was quickly absorbed; only very exceptionally did a very mild suppuration take place about them.

Experiment with cadaverin, according to Rinne and Grawitz, may be summarized as follows:

Solutions of cadaverin, free from bacteria, subcutaneously injected, produce according to their degree of concentration and value either a caustic action, or inflammation with termin-

ation in suppuration, or inflammatory œdema with subsequent resolution.

In $2^1/_2\%$ solution—or stronger—cadaverin completely kills the bacterial culture (staph. pyog. aureus) to which it is added. Weaker solutions in proportion to their strength delay or interfere with their growth.

Still further experiments have been made with ptomaine solutions to which living bacteria have been added. For this purpose pure cultures (gelatine and agar) of the staphylococci and streptococci were mixed with distilled water, and to this was added fluid in which had been macerated putrid meat, etc. This mixture was filtered and repeatedly sterilized, and then to it were again added fresh cultures of the aforesaid bacteria. Fluids thus or similarly prepared were experimented with in varying quantities. Small animals were found for the most part to be capable of disposing of 1 cc. of such mixtures without abscess formation, though local reaction was for the most part more acute than when pure cultures alone were used. In order to differentiate still better, pure cultures were injected upon one side of the animal's body, and pure ptomaine solutions upon the other. It seemed to make very little difference how the experiments were varied. Quantities up to 2 cc. seemed innocuous, even though injected into previously bruised tissues. Just where the line could be drawn between innocent or noxious amounts seemed to depend upon the particular ptomaine, its strength in solution, the kind of animal and its condition. It is Rinne's opinion, however, that ptomaines do, as it were, prepare the soil for bacterial attack, and that under their influence pus is more easily produced. In other words *under ptomaine poisoning of a certain degree of severity suppuration is favored and spreads*; but if this degree of toxicity is diminished or increased suppuration does not take place. If this toxæmia is combined with a traumatic lesion, suppuration may be quite circumscribed on account of a very lively cell proliferation by which a zone of protection is afforded.

Although, then, these artificial conditions thus produced in animals find no counterpart in man, they teach at least that pus production is not a specific action of one bacterium, but that local œdema, suppuration, necrosis and even sloughing

may be the occasional result of an irritation of a purely chemical character. The most important practical bearing of these facts experimentally elucidated is that by chemical means the normal resistance of healthy tissues may be reduced, and that the local condition, in such cases, is not so much a question as to the violence of the local lesion as of the resistance of the cells composing the tissues involved. Such a lowered resistance may be the result of local conditions, *e.g.*, frost-bite, mechanical strain etc., or very commonly of constitutional disturbances, such as struma, scurvy, gout, diabetes, syphilis, typhoid, scarlatina, diphtheria, puerperal fever, etc.

Take, for example, Lembert's and Kocher's researches concerning acute suppurative strumitis; they found it six times following after typhoid, three times after pneumonia, once after bronchitis, and once after puerperal fever, and also after acute gastro-intestinal catarrh. (*Deutsche Zeitschrift f. Chir.*, bd. x.) Five times along with the suppuration they noted putrefaction of the pus with formation of gas before opening the abscess. Furthermore they noticed that the thyroidal trouble did not begin during the general disease but as a sequel. Numerous other observers have noted the same feature in other manifestations of an analogous nature, as post-typhoidal phlegmons, etc. Thyroidal abscess is practically unknown as the result of injury alone; it results only from reduced vitality of the local tissues. For instance, thromboses, hæmorrhages, retrograde metamorphoses, in a goitre, constitute so many methods by which tissue resistance is diminished; to these may be added many constitutional conditions.

The thyroid is here taken merely as an illustrative organ; the same may be said of the bone-marrow, the liver, etc. The alimentary and respiratory passages offer open channels for infection, and after pathogenic organisms once enter the circulation they find their easiest prey in organs thus weakened.

In order to study more accurately the relations which ptomaine poisoning bears to the peculiar lowering of vital resistance that predisposes to suppuration, Rinne undertook a careful series of experiments based upon the intent to demonstrate:

a. Whether under otherwise similar conditions certain portions of the body developed differences of reaction under artificially produced toxæmias. For this purpose the peritoneum and the knee-joint were selected; the latter for the reason that invading cocci seem to be longer tolerated in the synovialis,

and consequently have more time for multiplication. It was necessary further to determine

b. Whether circulatory disturbances such as hyperæmia and œdema, which could be produced by ligating veins, prepared the soil for such infectious organisms; and

c. Whether trophic disturbances, such as might be caused by division of nerve trunks, exerted any influence upon the development of bacteria. The experiments were so arranged that infection was produced as well by indirect contamination of artificially induced thrombi as by direct introduction of microbes into the veins.

The inferences which can be legitimately drawn from his experiments are as follows:

Through the absorption of putrid and infectious material open wounds which show a tendency to heal have this tendency so far changed that they permit the action of saprophytic organisms from the surrounding atmosphere. His experiments did not show that any localization or infection took place from such pyogenic cocci as were introduced into the circulation.

Consequently such irritative agents as affect open wounds, in such cases, come from without the body rather than from within. In other words the internal condition is one of lower resistability, which makes the external lesion a *locus minoris resistentiæ* so far as micro-organisms from without are concerned. But in the wounds which exhibited these phenomena, the bacteria which had been injected were never recognized in the discharges; such appeared to come only from the air.

The conspicuous part which thrombi play in both physiological processes and pathological disturbances is well known. Surgical experiences dating back to the pre-antiseptic days richly teach the disasters due to breaking down of thrombi in suppurating and putrefying wounds. Secondary hæmorrhage alone, from this disease, has been in time past the cause of a large mortality rate.

Degeneration of intra-venous clots in cases of periphlebitic phlegmons is even more frequent, and is an important part of the pyæmic process. Any experiments, therefore, which shed additional light upon the subject of the infectiousness of thrombi should be hailed with delight. Thrombi are inten-

tionally produced at times, as after ligaturing vessels, either in their continuity or after their division; and they form as result of contusions and similar injuries, after frost-bite, etc. It is of great importance to learn how such thrombi behave toward cocci circulating in the blood, and whether they are so far attacked by the latter as to break down into pus.

To this end Rinne undertook another series of experiments by which thrombi were formed in various artificial ways, which clots he later sought to affect by pure cultures and putrid fluids introduced by various channels. Migration of pyogenic cocci into these thrombi, or into the pulmonary emboli thereby caused, was not to be detected in a single instance. Whether the animal was suffering from existing phlegmon or abscess, or whether it was so poisoned with putrid material that it died, seemed to make no difference; *thrombi* which were *not exposed to the air* were *not invaded by the pyogenic bacteria*. Hæmorrhagic infarcts did not occur in the lungs, and pulmonary emboli caused no appearances of metastatic inflammation. If infected emboli were deliberately used in the experiment in quantity then gangrene of the lungs followed; if their number was small then each tiny embolus seemed to become encapsulated by a proliferation from the intima of the vessel in which it lodged. Something similar was observed by Panum in 1862, who found that small toxic emboli were encapsulated.

Thus from Rinne's investigations it appears that neither such thrombi from ligature of veins, nor the areas immediately adjoining pulmonary emboli, nor the clots in the pulmonary arterioles resulting from emboli, nor lesions of the intima caused by deliberately injuring it, by themselves constitute in any sense points of predilection for the activity of pyogenic cocci. That is such thrombi and emboli as are protected from contact with the air do not constitute favorable soil for pyogenic bacterial invasion.

In confirmation of these statements we have others by different investigators: thus Wegner (*Experimentelles z. Lehre von Ovariotomie, Archiv. f. klin. Chir.*, xx), claims that blood effused into the peritoneum does not decompose if air be not admitted. And Mikulicz (*Archiv. f. klin. Chir.*, xxii) has declared blood clot to be a poor soil for development of coccobacteria septica. Thus from several independent sources it is made to appear that blood clot alone, without access of oxygen, offers no attractions for the bacteria of the septic state.

III. *Subcutaneous suppuration where there had previously been inflammation or some other disturbance.*—When a joint which has become anchylosed as the result of previous rheumatic synovitis or of epiphyseal ostitis, and about which there are no present signs of inflammation, undergoes *brisement force*, and then without the slightest external lesion suppurates, and when, as often happens, the pus is of the ichorous variety, we evidently have to deal with a case which belongs in a class by itself, since contamination by bacteria through the unbroken skin is excluded from the possibilities of the case.

Cases with small abrasions of the skin, with ecchymoses of the skin, or with superficial hæmatomata are not included in this class. Such cases have been reported by numerous authors (*e. g.*, Volkmann and Oberst, *Centralblatt f. Chir.*, 1885, Nos. 15 and 21; Müller, in Bruns' *Beitr. z. klin. Chir.*, iii, 2; Gussenbauer, *Deutsche Chirurgie*, Lief. 4, p. 125 *et seq.*; Köhler, *Charite-Annalen*, iii, p. 464; Rinne, *Archiv. f. klin. Chir.*, xxxix, p. 71), and one case in the writer's own experience has demonstrated to him their occasional occurrence. For their explanation two working hypotheses have been advanced: The first that some infectious material, living or inert, gains entrance into the circulation through the respiratory or digestive tracts, and thereupon finds in the spot affected a *locus minoris resistentiæ*; the other, that at that spot spores of the previously active germs have remained dormant, hibernating as it were, till some peculiar and favoring conditions could favor their reactivity.

In an address before the Philadelphia Pathological Society, in April, 1889 (*Am. Jour. Med. Sci.*, 1889), the writer alluded at some length to this latter theory as furnishing the key to certain problems in the study of acute infectious processes in bone, and towards it, as being equally explanatory of other clinical facts not relating to the osseous system, both the experiments of many investigators and the general consensus of opinion more and more point.

In the endeavor to elucidate this subject Rinne carried out further experiments as follows:

He operated on five dogs by introducing in their subcutaneous tissues worsted threads, most of which had been steeped in putrid solutions or pure cultures, or both. At the same time he introduced sterilized threads into their knee-joints. Nine or ten months later these animals, all of which survived the first procedure, were again subjected to endeavors to bring about infection by daily injecting into their abdomens active cultures of the pyogenic cocci, while they were at the same time fed with putrid meat or had subcutaneous injections of putrid fluids. At the same time mechanical injuries were inflicted on those parts of their bodies where lay the foreign bodies introduced months previously; they were contused or bruised, in the expectation that under the influence of the new infection acute abscess would be there and then produced. Astonishing amounts of putrescent and putrid material were ingested or injected.

The following results were obtained: At the points where lay the old foreign bodies, both in the tissues and the joints, in no instance was fresh inflammation discovered. At places where bones had been broken there was no suppuration. Subcutaneous peri- and intra-articular hæmorrhages were not infected, though the animal succumbed to septic infection, although a penetrating joint wound, though made with antiseptic precautions, suppurated. Artificial thrombi were not affected. Their peritoneums withstood numerous injections of large quantities of cultures of pyogenic cocci (Staph. pyog. aureus) without recognizable alteration. Even the pulmonary infarcts caused by small shot, by minute pieces of rubber, or by worsted fragments, did not evince the clear types of hæmorrhagic infarcts. The regions involved in the infarct areas still contained air. The foreign bodies were encapsulated by proliferation from the intima. Emboli produced by infected worsted seemed to cause gangrene locally in proportion to the amount of infectious material which they carried with them. A fragment, 1 ctm. long, was encapsulated without reaction like an inert foreign body, although it was saturated with infectious material.

These experimental results are consequently negative in shedding the desired light ; they serve to show, however, the wonderful powers of resistance possessed by certain animals. In spite of their significance in veterinary or comparative pathology we must, nevertheless, accept the teachings of clinical experience in diseases of man, since nothing appears much more certain than that recedives of suppurative and septic trouble occur in old foci of previous disease of similar nature, or localities not far distant.

In an inquiry of this character one easily reaches a limit beyond which investigations fail to give the desired information. Some of our most characteristic cases of this class occur as sequelæ of typhoid or some other of the infectious fevers. These fevers we cannot reproduce in animals, and, consequently, we cannot imitate in the laboratory the condition which so concerns us in the sick room. Again, it seems next to impossible, some say quite so, to produce a typical form of acute infectious osteomyelitis in such animals as we use for experimental purposes. Our closest laboratory imitation of this disease in man lacks some of its essential features, and it seems to be almost absolutely impossible to produce it in any such way as that in which clinical histories imply that it appears. For instance, Rinne endeavored, upon 11 different dogs, by first poisoning them with various putrid products and then contusing their bones, to reproduce some of the well known characteristics. Not once did suppuration occur. In certain experiments of my own, in the same direction, though fewer in number, I have had the same negative result.

IV. *A fourth group* may, perhaps, be made of cases of so-called spontaneous suppuration in previously healthy persons, who have never had any suppurative nor infectious disease.

Thus Bruns (*Beitrage z. klin. Chir.*, i, 237) not long since reported two cases of subcutaneous spiral fracture of the femur which suppurated; both cases died of septicæmia. One presented peculiar features. Aside from the spirally broken femur there was a compound fracture of the tibial head, the knee being widely opened. The opened joint and the compound fracture were treated according to the best antiseptic principles throughout the course of the case, and showed not the slightest disposition to pus formation. But the subcutaneous fracture was surrounded by a quantity of pus. Not the slightest skin lesion was found about the limb.

Quite recently also Steinthal reported two observations (*Deutsche med. Woch.*, 1887, No. 21) bearing on this subject.

One was a fracture of a femur about which a large abscess developed and was opened 4 weeks later; the patient died of septic trouble and metastatic suppuration. The other case was one of old dislocation of the hip, in which efforts to reduce re-

sulted in fracture of the neck of the femur. Five weeks later incision evacuated a quart of stinking pus with the necrotic head of the femur. The patient recovered. Steinthal thinks that in the first case infection took place through the lungs, and in the latter through the intestines, since the patient suffered from diarrhœa, which was in large measure due to such diseased teeth that he could not masticate properly. He does not seem to have thought of the possibility of infection through the decayed teeth. (Vide case on page 28 of Stimson's "Dislocations.")

In endeavoring to account for these cases we must not forget how easily slight abrasions of the skin may be overlooked, or, perhaps, healed before our examination; nor the fact that a contused and bruised, though unbroken skin, may not offer perfect protection against the penetration of germs from without. The difficulty of studying the subject is much enhanced by the rarity of such cases as those just alluded to. In the effort to elucidate it Rinne formulates a question about as follows :—Is it possible that in such cases bacteria, entering the healthy body by whatever channel they may, can segregate themselves in the subcutaneously injured tissues?

If an exact answer can be given to this query much of the mystery attending spontaneous inflammation and suppuration is cleared up.

Wyssokowitsch (*Zeit. f. Hygiene*, I.) investigating the fate of micro-organisms when injected into the blood of warm-blooded animals, demonstrated that most of them vanished in a short time, while a certain group, varying according to their variety and the quantity in which they were introduced, increased and multiplied up to the time of the animals' death. In this latter group he placed the staphylococcus aureus.

It has been further shown by Passet and others that of the pyogenic cocci these staphylococci aurei after incorporation into the body can exist—according to circumstances—in the blood and tissue juices, in an active state, for great lengths of time. They may be then eliminated, by which convalescence or recovery are established, or they may settle in some particular locality and determine suppuration, or after rapid reproduction and ptomaine formation the animal or patient may succumb to general infection, without displaying any localized pus production. It would seem as if a subcutaneous injury should act as a *locus minoris resistentiæ*, and that if any bacteria had gained access to the circulation they would have easy access to the lesion. Such would be an easy way to explain accidents like those suppurating fractures mentioned above. Rinne planned and carried out a long series of experiments well calculated to show that subcutaneous mechanical lesions either were or were not ordinarily such *loci minoris resistentiæ*. All sorts of injuries were in-

flicted and all sorts of irritating and infectious material were introduced or injected. For instance, a sponge as large as a hen's egg was cleaned and sterilized and then infected with twenty drops of fresh pure fluid culture of staphylococcus aureus. The abdomen of a dog was then opened, this infected sponge buried there, and the wound carefully closed. At first fever, vomiting and loss of appetite disturbed the animal, but it fully recovered in six days and remained well. Three months later at autopsy there was no evidence of peritonitis. In the omentum was a tumor, which consisted of the sponge surrounded by a fibrous capsule 1 ctm. thick. *Cultures* from the substance of the sponge *returned luxurious growth of the same staphylococcus aureus.*

Similarly endeavors to establish a focus in the kidneys, by exposing one and drawing through it a piece of wool and leaving it there, closing the wound antiseptically and then injecting elsewhere pyogenic cultures or putrid material, were equally unsuccessful.

Apparently, then, this question as to the localization of bacterial activity at the site of mechanical lesions must receive a negative answer. One is astonished to find how little evidence of local action appears on section of the tissues at the point in question. After scores of such apparently crucial experiments it is noted that nothing was found here. Intentional lesions quickly healed, foreign bodies encapsulated, hæmorrhages resorbed, and not once was local suppuration observed. The clinical experiences of every surgeon afford many parallel instances.

Rinne, more than any one else, has called our attention to this aspect of the subject, that the pathological importance of the pyogenic cocci has, perhaps, been greatly overestimated in this respect, *viz.*, not merely whether they *can* produce pus, but whether they invariably *do* or *must.* Herein lies a vast difference. After their discovery some were inclined to grant them a specificity akin to that of the erysipelas germ. But of late these views have somewhat modified. Rosenbach and still more Passet, showed how frequently the staph. pyog. alb. and aureus., less uniformly the strept. pyog., produce abscess formation. But we see, sometimes, reactionless absorbtion follow, and sometimes fatal blood poisoning, after injecting the same organisms. The researches of Grawitz and de Barry concerning purulent inflammation were enough to limit the specificity of these cocci. Then Scheurlen, Fehleisen, Bumm and B. Fraenkel confirmed their conclusions, in the main, and showed that the role of pyogenic cocci in causing progressive

suppuration is really a limited one.   It has been made neces-
sary for us to seek further for contributing causes of suppura-
tion.

In 1887 (*Tageblt. der Natur-forsch. Versamml. zu Wiesbaden*,
1887, p. 157) Rinne formulated the following conclusions :

1. Animal bodies have the capability of eliminating pyo-
genic cocci, when these, after introduction into the tissues, are
protected from direct contact with oxygen.

2. A migration of cocci in a subcutaneous injury, or in a sterile
abscess produced by injection of sterile chemicals, does not
occur, nor does it, after injection into the circulation or the
peritoneum.

3. Even after direct injection into fresh cutaneous wounds,
into young or old cicatricial tissue, or around foreign bodies,
there is no suppuration. .

4. It, therefore, follows that tissue lesions which determine
inflammatory reactions, at least, do not predispose for metas-
tatic suppurations ; nor do thrombi.

5. But it is comparatively easy to convert such lesions into
loci minoris resistentiæ by introduction therein of the chemical
products of bacteria.   Such a *locus* is any tissue whose nor-
mal resistance is lowered by any chemical or mechanical le-
sion; but so far as acute inflammations are concerned they do
not constitute—of necessity—such *loci* by any means.

Hence arises an inquiry of immense importance.

What sort of injury to a tissue is necessary in order to
so lower its power of resistance as to predispose it to bacterial
invasion?

From the failure of experiments already sufficiently indi-
cated it becomes evident that this inquiry needed to be directed
along other lines. Still working at the subject Rinne adopted
a somewhat different plan of action, and endeavored now to
introduce the bacterial material directly into the injured area
after inflicting a lesion.   *A priori* it would seem much easier
to thus convert such an area into a suppurative focus.   These
experiments comprised such procedures as the following:

Subcutaneous sections of tissue; immediate injection of bacteria into the section
thus made.

Subcutaneous introduction of glass balls filled with bacterial cultures; time for healing or encapsulation given; then, the balls being broken, liberation of their contents; still later injection of cocci into the injured tissue.

Subcutaneous injections of infected fluids.

Injections of cocci into old scars.

Encapsulation of shreds of wool which had been saturated with pyogenic cocci; these were tried in the joints, peritoneum, subcutaneous tissue, etc.

These last were undertaken especially with a view to determine whether mechanical injuries to tissues with exclusion of oxygen predispose to bacterial proliferation; and only in this last series was suppuration produced at all, and here only when the wool threads were infected. Even then the suppuration was not progressive in character and the cocci seemed to starve very quickly.

It appears then that mechanical lesions, *in loco*, do not predispose to bacterial, *i. e.*, pyogenic, activity, in other words to phlegmonous processes, *provided* that the locality is protected from access of air, that is of oxygen. In subcutaneous injuries absorption takes place too rapidly for the cocci to have time to form ptomaines, to disturb the tissues or to proliferate. Even in cicatricial tissue and in the neighborhood of scars, there is no *locus minoris resistentiæ;* resorption even here is scarcely hindered. The quicker the resorption the less noxious the bacteria. Rapid absorption and lively tissue-cell proliferation are really both protective in high degree; the "battle of the cells" being the defensive feature of the latter. Therefore lesions which cause an inflammatory reaction by no means predispose to metastatic suppuration.

Mechanical disturbance can also afford to cocci previously present in the tissues opportunity to set up a suppuration, by gaining access to some foreign body penetrating the tissues, and there producing ptomaines by whose help the process is established. That such a process is purely local is brought about by the factors just mentioned above.

In further elucidation of the precise part played by purely chemical agencies—by ptomaines like cadaverin, or by caustics like ammonia or croton oil—which without bacterial help can provoke a muco-fibrinous exudate, Rinne carried out yet another series of experiments intended to show whether there could take place an emigration of microbes from other parts of the body into an inflammatory focus caused by such chem-

icals.   After producing such foci in various animals (dogs and rabbits) pure cultures of pyogenic cocci were injected:

  a. Subcutaneously at distant points.

  b. In the abdomen.

  c. In the circulation.

In no instance could these cocci be recognized at the point in discussion; not even when extensive phlegmon was produced at the point of bacterial infection.

The order of the lesions was then reversed, without altering the result.

When an actual necrosis of tissue was produced then sometimes a penetration of ordinary bacteria from the air was observed, but nothing more.

Sometimes along with the croton oil, cadaverin, etc., the pyogenic cocci were injected at the same time, and then acute phlegmon was often produced, along with partial skin gangrene, and then the above cocci would be found along with other forms.   But more often the result was a severe caustic action with extended necrosis and then mummification.

From these it appears that such chemicals of themselves produce no spot of least resistance for pyogenic cocci; and further that ammonia or cadaverin, when sterilized, may

  1. In a certain concentration produce abscesses with sterile pus (puruloid).

  2. Or prepare the soil for bacteria which are injected with them.

  3. Or by destroying the overlying skin permit access of any of the organisms from the air; but that *they cannot* open the pathway for bacteria from the blood of the same individual; the explanation for which is probably to be found in a very lively cell proliferation.

Accordingly while it thus appears that chemically produced lesions do not predispose to bacterial activity, it further is seen that just as little also do the subcutaneous inflammations thus produced favor metastatic suppuration or become *loci minoris resistentiæ.*

Finally Rinne propounds this query: Wherein lies the key to the comprehension of those cases where abscess occurs

without our being able to recognize any disease or point of infection?

Everything points to the impossibility of a purely spontaneous suppuration, as well as to the complex character of various contributing factors. And first of all the histories elicited are seldom of value enough to shed real light, and examinations of patients are seldom scrutinizing enough.

Then it must be remembered that the lesion permitting entrance of bacteria may be healed before the abscess comes under observation; *e. g.*, pelvic abscesses or endocarditis puerperalis ulcerosa some time after puerperal fever, etc. Thus Grawitz reported to Rinne a case where a purulent basilar meningitis was traced along the second branch of the trifacial nerve, and found to have its origin in a furuncle just over the infra-orbital foramen, which had almost healed.

Moreover the primary lesion may present no clinical signs and so be passed unnoticed; *e. g.*, the abscesses or meningitis known to follow pneumonia. Probably so-called idiopathic peritonitis or pleuritis, like the so-called rheumatic, come under this category.

Acute infectious osteomyelitis was formerly regarded as a purely idiopathic disease; now we know that it is a staphylococcus infection, but sometimes find it difficult to trace the path of infection. It may follow typhus, scarlatina and diphtheria, or perityphlitic or pelvic abscesses, for instance, which may have been long past; or it may follow some external furuncle or phlegmon.

But it often happens that the septic or suppurative process has reached its height when the case first comes under accurate observation and that the lapse of time has obliterated in one way or another those evidences which might lead to a more speedy and accurate recognition of the prime causes for which we seek. Previous "feverish states" offer a much more plausible explanation for many cases of so-called spontaneous suppuration than do the majority of histories of injury.